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19. ABSTRACT (Continue on reverse if necessary and identify by block number)

This project involves a study of electron transfer through double-stranded DNA to determine whether the configuration of the stacked bases in DNA can facilitate the transfer process over long distances. We will attempt to define the length, sequence, and conformation dependence of these transfer rates through DNA. The results of these experiments will hopefully lead to practical methods for deciphering as electronic signals the information content coded in DNA.

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| 22a. NAME OF RESPONSIBLE INDIVIDUAL: Dr. Michael Marron | 22b. TELEPHONE (Include Area Code): (202) 696-4760 / 22c. OFFICE SYMBOL: ONR |

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Date: 1 June 1989

Annual Report on Contract N00014-88-K-0388

Principal Investigator: Pui Shing Ho

Contractor: Oregon State University
Contract Title: DNA mediated electron transfer and application to 'Biochip' development

Contract Period: 1988 June 1 through 1991 May 31

Research objective: To determine whether double stranded DNA can mediate the rate of electron transfer from a donor to an acceptor and whether the transfer rates are dependent on the length, base sequence and conformation of the intervening DNA. These studies will form the basis for determining whether DNA may be used as the primary matrix for designing a biological microprocessor, or 'Biochip'.

Progress (Year 1): In the first year of this contract, we have synthesised and purified a series of oligonucleotides for the proposed electron transfer studies. The sequences d(CACG) and its complement d(CGTG), d(CGCACG) and its complement d(CGTGCG), and d(CGCGCACACGCG) and its complement d(CGCGTGTGCGCG) were synthesized on an Applied Biosystems DNA synthesizer for the length dependent electron transfer rate measurements. Each sequence was purified using an ISCO HPLC system, with a C18 reverse phase column. From this, we have synthesized the 5' ethylene diamine derivatives of each oligonucleotide (EDA-DNA) via an activated imidizole derivative and also, more efficiently, through direct reaction of the DNA with ethylene diamine in the presence of the coupling reagent (CDI). In addition, activated porphyrins have been synthesized including the N-hydroxylsuccinyl pyrroporphyrin (NHS-Por) as well as the ethylene diamine derivative of the porphyrin (EDA-Por), and the zinc (II) and ferric derivatives of each porphyrin. Each step during the synthesis has been purified by HPLC chromatography. The NHS-Por has been reacted with the EDA porphyrins as previously reported and found to yield the porphyrin derivatives of each oligonucleotide sequence. Data collection on these samples will proceed as soon as the flash photolysis apparatus is completely assembled and tested. Meanwhile, we are trying to optimize the final coupling step to increase the percent yield of the products.

We are assembling the components of the flash photolysis apparatus for measuring the electron transfer rates in the DNAs. The analysing beam has been assembled from components purchased from Photon Technologies, Inc. The analysing beam includes a high intensity quartz halogen arc lamp (200 W), a variable wavelength monochrometer, a light-tight sample chamber with temperature control, and a photomultiplier housing. A Hyundai 286C microcomputer was purchased to control the flash setup and to collect and analyze the absorption data from the electron transfer measurements. A FORTRAN program MING was obtained from Prof. Brian Hoffman, Dept. of Chemistry, Norhtwestern University, Evanston, IL, and was subsequently modified for data collection and analysis on the flash apparatus. The program completely automates the initiation of the excitation of the electron donor, control of

an electronic shutter that blocks light from irradiating the sample, initates data collection, and analyses the data after collection in terms of simple first order and several double exponential decay models. We are awaiting the final testing of the interface that allows communication between the microcomputer and the flash apparatus.

Work Plan (Year 2): In the second year, we plan to complete the assembly and testing of the flash photolysis apparatus and programs. Once this is complete, we will begin the studies to measure the length dependence of electron transfer reactions through the DNA oligonmers. We will also start to synthesize the modified oligonucleotides required to study the sequence dependence of these electron transfer rates.

Inventions: None

Publications: No publications have resulted directly from the first year studies. We have, however, completed a study on the crystal structure of a uridine containing Z-DNA hexamer that was considered to be partially funded by this project. The results of this study has been submitted for publication to Nucleic Acids Research under the following title: 'Stabilization of Z-DNA by demethylating thymine: 1.3 Å structure of d($m^5$CGUA$m^5$CG)', G. Zhou and P.S. Ho.

Training activities: There are currently two graduate students working on this project and we have had three undergraduates working intermittantly on the synthesis phases of the project. The two graduate students are Mr. Guangwen Zhou, a third year Ph.D. candidate, and Mr. Todd F. Kagawa, a second year Ph.D. candidate. Mr. Zhou, a citizen of the People's Republic of China, has a good background in physics and has already shown made remarkable progress towards his degree. By the end of this summer, he will have written and submitted his sixth paper. Mr. Kagawa, a citizen of the U.S.A., is strong in chemical synthesis and purification techniques. He is also first author on a paper recently accepted for publication in Biochemistry concerning the theory behind the thermodynamic difference between various sequences as B- and Z-DNA. A third graduate student, Mr. Bernhard Geierstranger, an M.S. candidate whose funding is from a Fulbright fellowship and who is a citizen of the Federal Republic of Germany, will begin working with us this summer. His interests and abilities are in chemical engineering, and he should contribute significantly to the success of this project.

The demographic data you have requested regarding these students are:

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| Women and minorities: | 0 |
| Non-citizens: | 2 (Peoples Republic of China and Federal Republic of Germany) |

Awards/Fellowships: None